

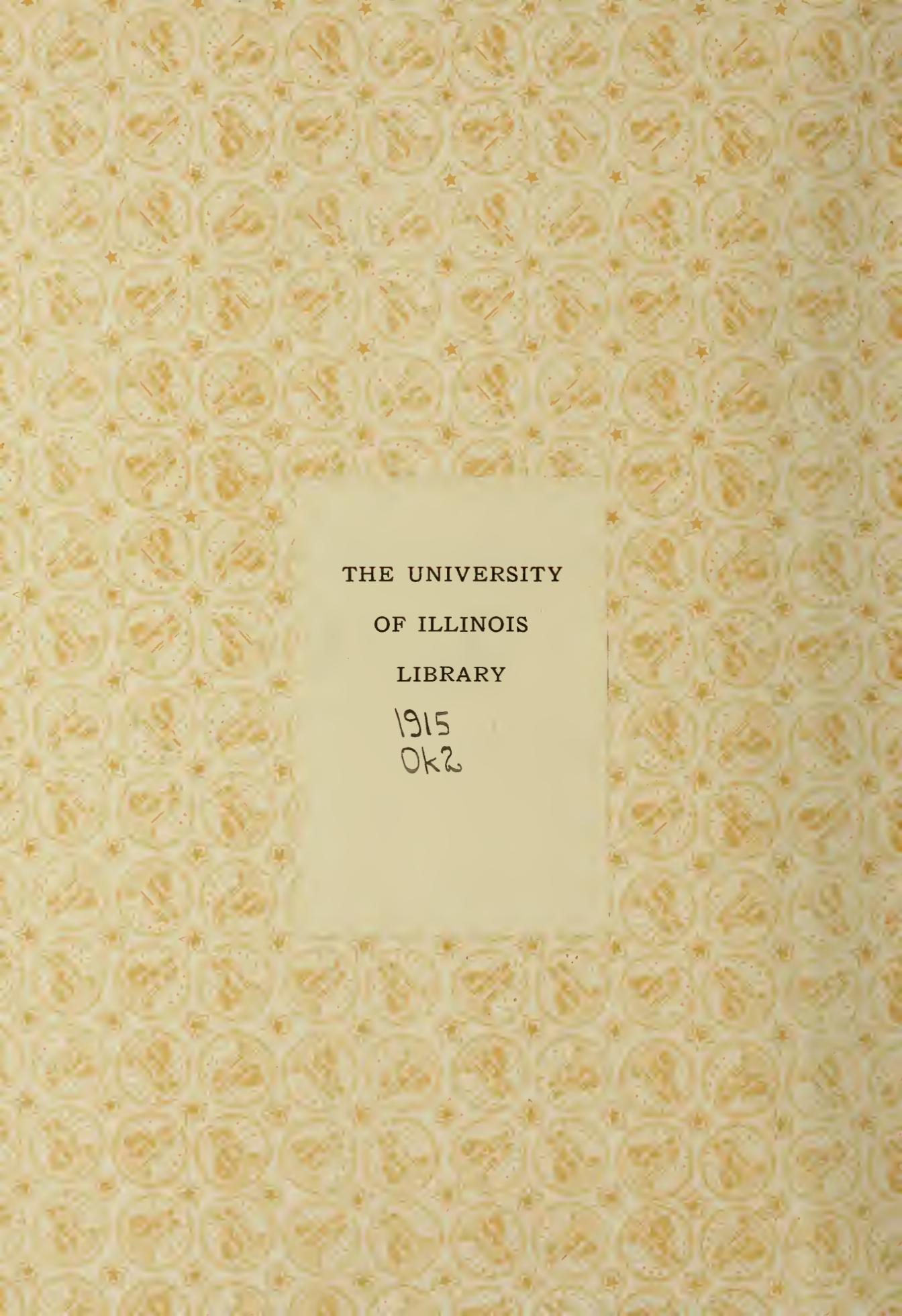
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The Identification of  
Drugs Containing Emodin

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THE IDENTIFICATION OF DRUGS  
CONTAINING EMODIN

BY

RUTH ELIZA OKEY  
B. S. Monmouth College, 1914

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THESIS

Submitted in Partial Fulfillment of the Requirements for the

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IN

THE GRADUATE SCHOOL

OF THE

UNIVERSITY OF ILLINOIS

1915



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May 31, 1915. 190

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

Ruth Eliza Okey

ENTITLED The Identification of Drugs Containing Emodin.

BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

DEGREE OF Master of Science in Chemistry.

*George D. Beal*

In Charge of Major Work

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Recommendation concurred in:

Committee

on

Final Examination



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## Identification of Drugs Containing Emodin.

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\*\*\* HISTORICAL \*\*\*



## IDENTIFICATION OF DRUGS CONTAINING EMODIN

### A. Historical:

More or less has been known about the medicinal properties of these drugs since the beginning of the middle ages, but the work on the chemical constitution was, practically, begun in the nineteenth century.

Gerber made an analysis of frangulin in 1828, Bley separated aloes into a number of resins in 1832; and in 1834 we have a discussion, by Geiger, of the chemical analyses of rhubarb made before that time. Probably this discussion served for an example to his successors, for the chief point that he makes is that all the "active principles" isolated up to his time are highly impure, and that his "rhabarber gelb" is the true active principle. It is interesting to note also, that he recognizes the identity of this active principle and that obtained from rumex, and that he mentions the preparation of a substance called rhein by Vaudin, several years before.

In 1836 Schrader and Herberger discovered and studied a "chrysophanic acid" and in the same year O. Henry made a complete analysis of rhubarb; finding "rhabarber gelb" or rhein, a bitter, a fatty oil, tannic and pectic acids, sugar, starch, albumins, gums, Ca oxalate, and sulfate, iron, and phosphoric acid. The next work was that of Brandis (1839). He described and gave the formula for a "rhabarber säure", but he failed to make any connection between this and rhein. Two years later Dulk prepared a rhein from rhubarb, but, like all the other preparations of this date, his product was undoubtedly a mixture of anthraquinone derivatives and other things.



The action of nitric acid on aloes was studied by Schunk (1841 to 1843). He describes four N containing acids; aloetic, aloeresinic, chrysophanic, and, chrysolephinic acids. Buotin (1842) gave aloetic acid the formula  $C_{15}H_7N_4O_{12}$ .

Büchner and Robinquet made analyses of aloes in the next two years recognizing the aloetic acid mentioned above.

About 1859 Smith and later Stenhouse prepared a crystalline body from aloes, which they called aloin. Their work is to be noted because they studied the action of acids on this substance and prepared the bromine derivative.

At this same time (1845) Schlossberger and Döpping analysed rhubarb, finding resins, extractives, and a chrysophanic acid which they recognize as identical with that prepared by Rochleder and Heldt (1843) from *Physcia parietina*, as well as the rhein of Geiger, and the rhabarber-säure of Brandis. It is hard to estimate the purity of the compounds prepared by these early investigators, but the fact that Rochleder's analysis checks that of Schlossberger to hundredths of a per cent points to careful work in the separation of the compounds.

Biswangen (in 1849) found an amorphous yellow coloring matter in the bark of *Rhamnus Frangula*, which was later (1853) prepared by Büchner as yellow needles, soluble in alcohol and ether. Büchner named this substance rhamnoxanthin; its resemblance to the cathartin of senna leaves having previously been noted by Biswanger, who had named the bitter principle from *Rhamnus cathartica* rhamnocathartin, in order that the two might be



distinguished. Büchner noted that these substances are soluble in ammonia and in fixed alkalis with a purple red color; also that they are soluble in concentrated sulfuric acid with a red color; the substances being thrown down by dilution or by neutralization as yellow precipitates.

Casselman (1857) made the first ultimate analysis of a derivative from frangula which he called frangulin. He said that Buchner's material was impure, and gave as the melting point of pure frangulin (240°) formula:  $C_6H_4O_3$ . He also obtained a 5N derivative and concluded that this was formed, together with oxalic acid, when he treated frangulin with fuming nitric acid.

Philipson (1858) recognized the rhamnoxanthin of Büchner, noting also that when treated with concentrated sulfuric acid, it turned emerald green - a color which soon disappeared, while the substance dissolved purple red, if the acid was not immediately decanted.

In this year (1858) De la Rue and Miller analyzed rhubarb; obtaining a chrysophanic acid which agreed exactly with Rochleder and Heldt's analyses. Their most important contribution was, however, the isolation of emodin, for which they obtained the melting point, 250°, but for which they gave no formula. They described this substance as soluble in alcohol, gl. acetic acid, amyl alcohol; and giving a purple red solution with ammonia and fixed alkalis.

Buchner and Herberger (1858) prepared a rumicin from the roots of *Rumex obtusifolius*, which they considered the same as the chrysophanic acid of Rochleder and Heldt, differing from it in melting point only.



Kossman (1858) divided aloin into two bodies, one soluble and the other insoluble in water, which he called aloetic and aloe resinic acids.

Kubly (1866) found in *Rhamnus frangula* a glucoside called avornin, which he split into a sugar and an acid which he called avornic acid. This glucoside was probably identical with the frangulin of Casselman, but Kubly was the first to demonstrate its glucosidic nature.

Batka (1864) found in senna leaves, besides chrysophanic acid; legumin, gum, sugar, sennacrin, sennaretin, sennatannic acid, and oxalic acid.

Büchner and Kubly (1866) declared the active substance in senna leaves to be a glucoside, which they hydrolyzed to cathartic acid and a sugar.

Bourgoin and Bouchut (1866) recognized besides chrysophanic acid, two active principles, which they called cathartin and cathartic acid.

Dragendorff (1872) gave the following tests for aloes:

Pb Ac ..... Greenish black precipitate.

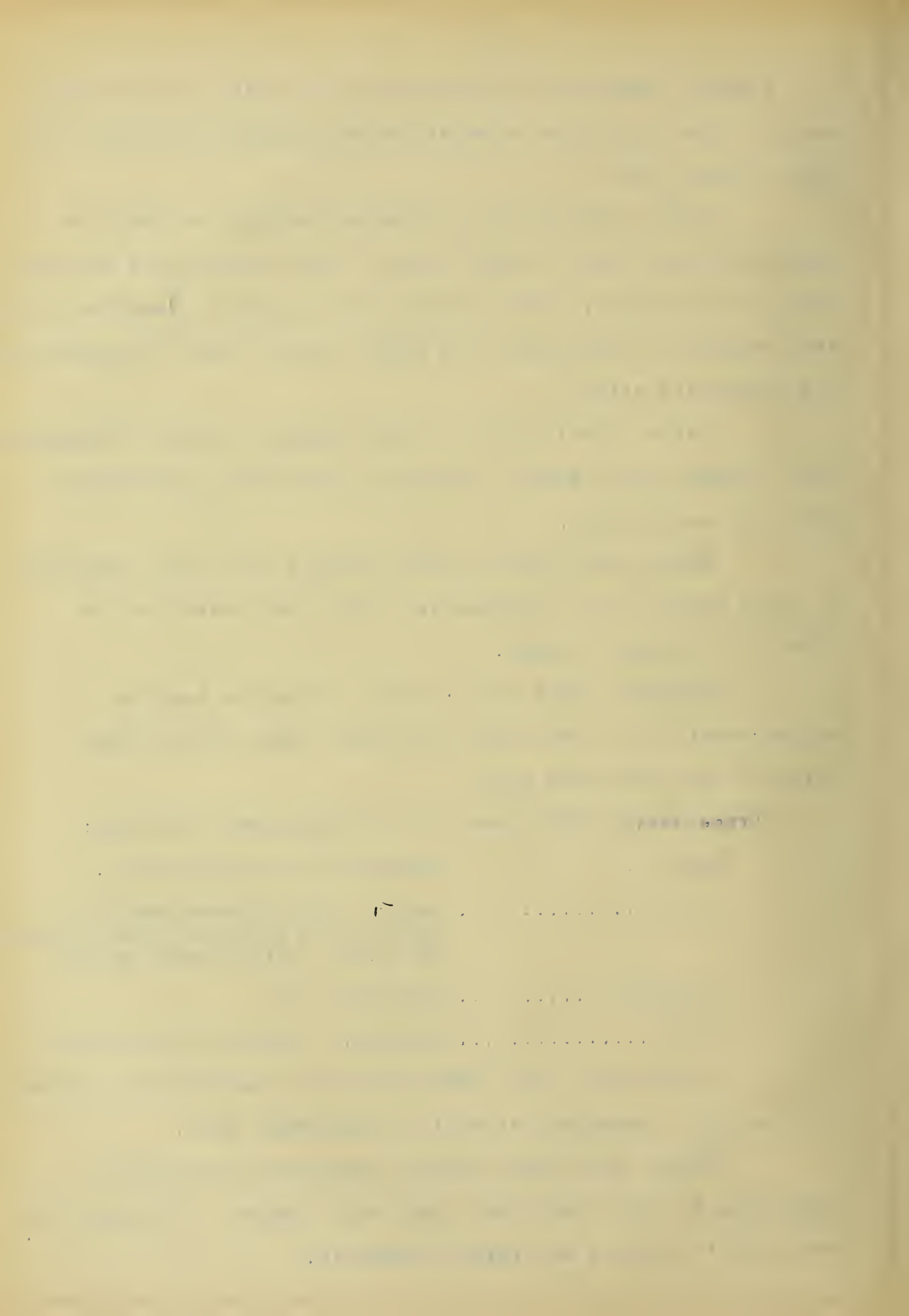
Pt Cl<sub>4</sub> ..... Red to violet (Barbadoes and Curaco) and greenish brown (Socotra and Cape) Yellow brown (Natal)

AuCl<sub>3</sub> HCl ..... Raspberry red.

HgNO<sub>3</sub> ..... Reddish. (Curaco and Barbadoes)

In the same year Tilden prepared a substitution product of aloin with chlorine, as well as chrysammic acid.

Faust (1872) made another analysis of frangulin, separating it into frangulinic acid and a sugar. He pointed out that Kubly's avornin was impure frangulin.



Schmidt (1875) prepared methyl anthracene by the reduction of aloes. This is probably the first proof of the fact that these drugs are anthraquinone derivatives. The next year Liebermann deduced as a formula for emodin  $C_{14}H_{10}O_5$  or  $C_{17}H_5$   $\left\{ \begin{array}{l} CH_3 \\ (OH)_3 \\ COOH \end{array} \right.$

The same year, Liebermann and Waldstein pointed out the identity of emodine and Faust's frangulinic acid; and a year later Liebermann, in a paper on the anthraquinone group, gave the dihydroxy anthraquinone structure as that of chrysophanic acid, and declared that tetranitro-chrysophanic acid was not identical with chrysammic acid.

Tilden (1877) obtained a crystalline oxidation product by treating aloin with potassium bichromate in concentrated sulfuric acid.

Prescott (1879) made a chemical analysis of the bark of *Rhamnus purshiana*. He obtained a crystalline body from his dilute alcohol solution, but he considered this a result of his method of treatment. He points out, however, that his resins probably contain emodin. He also made an analysis of *Rhamnus frangula*, obtaining a red resin, a brown resin, and a yellow resin, the first two of which were soluble in KOH and sulfuric acid; the brown resin with a red color, and the red resin with a brownish red color.

Bornträger (1890) published his test for aloes, i.e., treatment of a benzene solution of a liquid containing aloes with ammonia, by which a red color was obtained.

Klunge in the same year published the following tests for aloes: Benzene, carbon bisulfide and chloroform extracts of



aloes, on treatment with ferric chloride became brownish black, on treatment with I in KI solution aloe hepatica became a red violet color, while with aloe lucida, only a slight tinge was obtained. These tests attracted a considerable amount of notice, to judge from the literature of the next few years. Lenz (1883) investigated the action on the resid from the amyl alcohol extract of aloes of Br in KBr, I in KI, PbOAc, and mercurous nitrate, as well as tannic acid; obtaining precipitates in solutions of this resid with all these reagents. He also gave the following test for aloes:

Evaporate the amyl alcohol extract of the drug to dryness on the water bath, take up with nitric acid, again evaporate. This residue, when treated with potassium cyanide in potassium hydroxide gives a blood red color. Lenz also pointed out that rhubarb, frangula and senna respond positively to Borntragers ammonia test, and to the test with the iodine solution.

Cripp and Dymond (1885) published another test for aloes: To one grain aloes, placed on a glass mortar standing on white paper, was added 16 drops concentrated sulfuric acid. When this had dissolved, 4 drops nitric acid were added, and then one ounce of water, the presence of aloes being indicated by a color ranging from orange to deep crimson. He noted that rhubarb, rumex, senna, and frangula also respond to this test, but in very dilute solutions, ammonia does not turn aloes and senna pink, as it does rhubarb, cascara, and frangula.

Limoesin (1885) noted that the scraped surface of Cascara bark becomes red with ammonia.



Stockmann (1885) found as the active principle of senna, a tasteless cathartic acid, which, when boiled with acids or with potash, yielded glucose and a yellow resinous substance of purgative properties.

Schwabe (1888) found in frangula 0.04% frangulin and 0.1% emodin. He gave as the melting point of frangulin 228°; and stated that on hydrolysis it yielded emodin and a sugar, probably rhamnodulcitol. He found emodin, but no frangulin, in *Rhamnus purshiana*. Later he stated that he found no frangulin in fresh samples of frangula bark, and suggested that it was formed from emodin on standing. Meier and Webber (1888) found an enzyme in the bark of *Rhamnus purshiana*, and while they did not suggest this possibility, it seemed that if Schwabe had been right this might have accounted for the change.

Klunge in 1889 published his cupraloin test, which he applied by evaporating a small amount of extract to dryness on a watch crystal, taking up the resid with cold water, and treating the aqueous extract with a few drops of copper sulfate, a little NaCl, and finally, a few drops of alcohol; a red coloration indicating the presence of aloes. This seems to be the first aloes reaction published, that does not apply almost equally well to some of these other drugs.

Thorpe and his co-workers (1890 to 1892) analyzed frangulin, obtaining 67.6% emodin, also a small amount of an isomeric anthraquinone derivative. They succeeded, also in identifying the sugar of frangulin as rhamnose.

Schoutelen (1892) used as a test for aloes, a concentrated solution of borax with which he obtained a green



fluorescence on standing from 20 to 25 minutes.

LePrince (1892) analyzed cascara, obtaining as active principle; cascacin, in cryst. prismatic needles, tasteless, odorless, insoluble in water, m. 300', dark at 200'. Indications are that he had a mixture of substances.

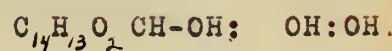
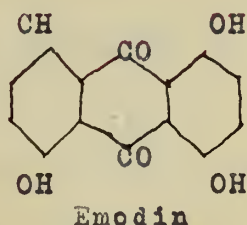
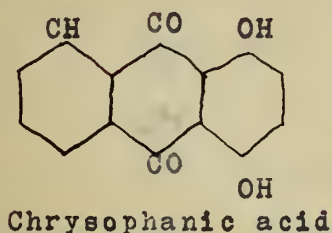
Dohme and Engelhardt (1897) found that Cascara Sagrada contained, not emodin as such, but a glucoside of emodin, which they called purshianin, and which was not identical with frangulin.

Anweng (1898) reported the separation of two glucosides from frangula on treatment of the resids obtained by evaporating a 60% alcohol extract with water; the primary glucoside so obtained being soluble in water and yielding 20%, while the secondary glucoside yielded 12% and was insoluble in water. Both, on hydrolysis yielded emodin, chrysophanic acid, sugar, and a substance which resembled Liebermann's rhamnetin, except that it was more soluble in water; and which the authors named frangula rhamnetin. They obtained it as a yellow sublimate in needle shaped crystals. The other product of hydrolysis was a principle soluble in alcohol and containing iron, which they called "eisen-emodin". Primary and secondary glucosides were also obtained from rhubarb and senna, but the glucoside from senna yielded only emodin and rhamnetin on hydrolysis.

Hesse (1898) revised his former analyses of rhubarb, stating that it contained chrysophanic acid, m. p. 186-188'  $C_{15}H_8O_2(OH)_2$  emodin, m. p. 259',  $C_{15}H_7O_2(OH)_3$ ; and rhein  $C_{22}H_{14}O_6(OH)_4$ , m. p. 262'. He also recognized rumicin as pure chrysophanic acid. A year later Hesse recognized another anthraquinone derivative



which he called rhabarberon, an isomer of emodin. He gave the following formulae:



Rhabarberon

Hesse also found chrysophanic acid and products which he called nepodin and lepodin in some varieties of rumex which he examined.

Several analyses of aloes were made in 1898. Dohme stated that the resin of aloes was an ester or organic salt, varying with the nature of the aloes, and that the variable constituent was the acid, the other being aloeresitannol. He also stated that aloes contained an emodin.

Pederson found 0.015% emodin in aloes, and stated that the resin was a para-cumaric acid ester of aloeresitannol.

Leger (1898) obtained aloe-emodin by hydrolysis of aloin with HCl.

The next year (1899) Kremel published a method of detecting aloes by nitrating and examining the crystals of chrysammic acid so formed.

LePrince (1899) made a new analysis of cascara, obtaining rhein, chrysophanic acid, emodin, and chrysarobin. From his description of chrysophanic acid, however, it appears doubtful whether or not he did find it, especially since he describes his product as soluble in ammonia.

Anweng-Barr (1899) published a method of separating



the glucosides of frangula, cascara and rhubarb by successive extraction with benzene, benzene and absolute alcohol, and 60% alcohol. These glucosides yielded on hydrolysis emodin, chrysophanic acid, and rhamnetin.

Tschirsch and Hiepe (1900) found in senna, senna-emodin, m.p. 223' to 224' chrysophanic acid, iso-emodin and rhamnetin and cathartic acid.

Oesterle (1900) stated that the emodins of aloes and frangula are isomers, and he distinguished between them by the following properties: Aloe-emodin melts at 223', is soluble in sulfuric acid with a red color, and it gives a green-yellow on pouring into water; the addition of ammonia to the water solution of this emodin produces a violet-red; baryta water, a rose color. The tri-benzoyl derivative melts at 235', the propionyl at 152-153'. Frangula emodin melts at 250', the sulfuric acid solution turns blue when poured into water; and cherry red with baryta water. The benzoyl derivative melts at 225', the propionyl at 121 to 122'.

Anweng (1900) found that the primary glucosides of rhubarb and cascara were emodin glucosides, while those from frangula yielded frangulic acid alone.

Oesterle (1900) made several experiments with the oxidation of the emodins of aloes and frangula, but he was unable to get out his products in pure form. He was more successful with reduction products, obtaining hydranthrons by reducing the glacial acetic acid solution with tin granules and hydrochloric acid.

Hirschsohn (1901) published the following tests for aloes:



10 cc. of a water solution, (1 \_ 1000) treated with one drop cupric sulfate solution (1-10) and one drop hydrogen peroxide; the mixture being heated to boiling, produced a red color. If K ferricyanide were substituted for the peroxide, a reddish brown color resulted. Curaco and Barbadoes aloes also produced a red tint with K-thiocyanate and Na-nitro-prusside.

Tschirsch and Hiepe (1901) obtained the following amounts of emodin from various drugs

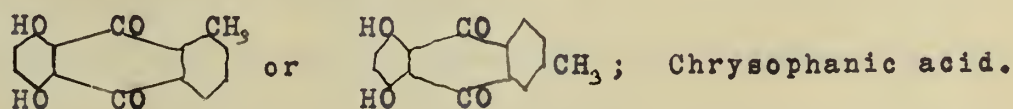
Frangula .....	2.6%	Cascara .....	0.61%
Rhubarb .....	1.5%	Cape Aloes .....	0.8 %

Tschirsch and Heuberger (1902) made new analyses of rhubarb, finding a mono-methyl ether of chrysophanic acid, as well as chrysophanic acid, rhein, and emodin. They gave to rhein the structure of a methylene ester of tetraoxy anthraquinone, based on the fact that rhein, on reduction with zinc dust gives anthracene, and, on acetylation, a diacetyl derivative.

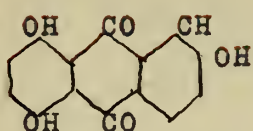
Tschirsch also made some rather unsatisfactory experiments on methods for putting the inert anthraquinone derivatives of these drugs into active form.

Oesterle (1903) obtained rhein from aloe emodin by treatment with equal parts  $\text{CrO}_3$  and glacial acetic acid. He did not, however, derive the acid formula from his results.

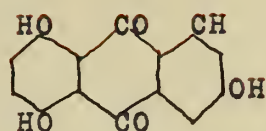
Jowett and Potter (1903) deduced the following formulae, disputing Hesse's placing of the OH groups in emodin on the ground that it yields a mono-methyl ester:







or



Emodin.

Jewett (1904) found in cascara bark: emodin, an isomer melting at 183°; dextrose, and a substance which, on hydrolysis yielded syringic acid. The glucosides present yielded on hydrolysis, emodin, chrysophanic acid and rhamnetin.

Hesse 1905-1908 prepared rhein, m. p. 312°. At about the same time Tschirsch and others analyzed rhubarb, grown in France and England, finding emodin, chrysophanic acid, and iso-emodin, but no rhein.

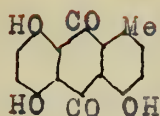
Tschirsch and Hoffbauer developed a method of estimating aloes, using 5% borax solution, and the cupraloin reaction.

Brissmoret and Combes, at about the same time, stated that Nickel acetate turned anthraquinones red, and that a chloroform solution of an oxychinone evaporated on filter paper, became red with ammonia.

Alvarez (1907), in a paper on the color reactions of organic compounds, described a method of testing drugs by placing in a porcelain capsule with 0.2 to 0.5g, Na peroxide (to 0.1g of the drug) and 5 cc alcohol. After 4 to 6 minutes, 15 cc water were added. Emodin developed an intense rose color, and chrysophanic acid a blue violet, which became brighter on dilution; as did also the dihydroxy anthraquinones.

Oesterle and Tisza (1908) found, from the behavior of the trimethyl esters of frangula emodin, the following formula which differs from the ones previously given in that none of the OH groups are assigned to the alpha position:





They also found the formula for carefully purified rhein to be  $C_{15}H_8O_4$ .

Lothian (1909) published a series of color-reactions obtained by treating solutions of aloin with various alkaloids. He stated that the red color be obtained is due, not to emodin, but to the aloins present.

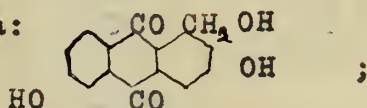
Robinson and Simonsen (1909) obtained rhein by the oxidation of aloin.

Oesterle and Tisza (1909) distilled frangula emodin with zinc dust, obtaining  $\beta$ -methyl anthracene, while from aloe-emodin they obtained a different hydrocarbon. Rhein, on similar treatment yielded anthracene. The next year Oesterle and Johann stated that the methylated substance with which chrysophanic acid in rhubarb is invariably associated, is emodin-mono-methyl-ether, identical with that associated with chrysophanic acid in *Rumex ecklonianus*.

Oesterle and Riat (1910) prepared aloe-emodin from aloin; forming the aloetinic acid by the action of nitric acid on aloin, reducing this, diazotizing, and boiling with alcohol. They conclude that aloetinic acid is therefore a nitrated aloe-emodin, rather than a tetra-nitro-methyl anthraquinone. Since they obtained methyl anthracene on reducing aloe-emodin with zinc dust; and rhein, on oxidation with chromic acid; and since they find that by oxidizing aloetinic acid with chromic acid, they obtain, on reducing with KHS, diazotizing while hot, and



purifying the compound so obtained through the acetyl derivative, a compound of the formula:



one of the OH groups in aloe-emodin is probably on a side chain. In the same year Oesterle and Riat succeeded in decomposing aloin, obtaining aloe emodin and a sugar by heating with alcoholic HCl or alcoholic sulfuric acid.

Leger (1910) obtained in addition to the chrysammic acid which had previously been isolated from the product of the action of nitric acid on aloins; a tetra-nitro-aloe emodin.

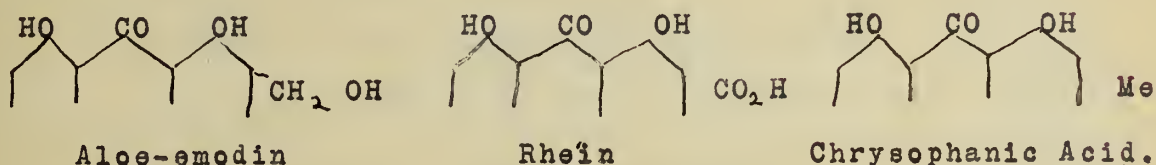
In the same year Kröber published a list of characteristics necessary to a good fluid-extract of *Rhamnus purshiana* and Alcock stated that the alcoholic distillate from an extract of *cascara sagrada* yielded a substance which gave positive results to the tests for emodin.

Tutin and Clewer (1910) made a detailed and very careful analysis of *Rumex ecklonianus*, obtaining, among other things, the anthraquinone derivatives: chrysophanic acid, emodin, emodin-mono-methylester, a sugar that yielded d-phenyl-glucosazone. This is probably the latest and best work we have on rumex.

Tutin and Clewer (1911) made a like investigation of rhubarb, finding, as a result of their analysis; chrysophanic acid, rhein, emodin, aloe-emodin, emodin-mono-methyl-ester, a new anthraquinone derivative, to which they gave the name, rheinolic acid,  $C_{17}H_{10}O_6$  m.p. 295-297° m; as well as a mixture of glucosides of rhein, emodin, aloe emodin, emodin-mono-methyl-ester, and chrysophanic acids.



Oesterle (1911) deduced the relationship between aloemodin, emodin, chrysophanic acid and rhein; basing a part of his evidence on the fact that aloemodin on reduction gave chrysophanic acid, and on oxidation rhein.



In the same year Oesterle also published a modification of the formula for frangula-emodin, based on the fact that, in the tetra-nitro derivative, two NO<sub>2</sub> groups are in the alpha and two in the beta position; and since the methyl group is in the beta position; there are only two alpha and one beta positions left for the hydroxyl groups.

Rosenthaler (1911) carried out a series of sublimation tests, heating the powders of various drugs in exhausted apparatus. He obtained results, which led him to group the anthraquinone - containing drugs as follows:

Sublimates have basic brown or yellow brown color, and give typical red purple with NaOH.

A. Sublimates contain isolated needles.

I. Skeleton-like form above, scales below.

Alcoholic solution with ferric chloride, reddish brown.

Rhei Rhapontici.

II. No skeleton or scales.

(a) Alcoholic solution with ferric chloride, green.

Folia senna.

(b) Alcoholic solution with ferric chloride, red-brown.  
Rhei.

B. Sublimates without isolated needles

(a) Does not melt on heating.



Contains columns, partly built up at angles of 45° and 90° with one another.

Alcohol solution stays green with ferric chloride.

Frangula.

(b) Sublimate without such needles.

Amorphous resin containing thin needles.

Alcohol solution with ferric chloride, first green, then brown. *Rhamnus purshiana*.

Kröber (1911) made the following distinctions between the fluid extracts of cascara and frangula: If the extracts are shaken with nine parts of water, cascara produces a flocculent precipitate that settles quickly, while that from frangula is muddy, and settles slowly. The filtrates from cascara gave precipitates with cupric sulfate, ammonium molybdate, Na Cl, HCl, nitric acid, sulfuric acid, acetic acid, and ferric chloride, while those from frangula did not. Shaken with dilute KOH cascara gave a brown froth, and frangula a rose colored one.

Mosler (1912) published a method for detecting aloes in the presence of drugs containing oxymethyl anthraquinone derivatives, subjecting the substance to be analyzed to an elaborate succession of precipitations to remove foreign matter, and then testing by Bornträger's reaction, bromine water, borax, and the cupraloin tests. He also stated that other drugs of the same sort might be distinguished by the crystalline form of the nitric acid derivatives.

Fischer and Gross (1912) prepared chrysophanic acid from chrysarobin. They state that, as usually prepared, it contains emodin mono-methyl ester, which is soluble in much the



same solvents.

Tutin (1913) made an analysis of senna, finding no anthraquinone derivatives except rhein, aloe-emodin, and their glucosides. This seems to be a proof of the small value of many of the earlier analyses of this drug; for Tutin offers evidence which appears to be good, and it directly contradicts the statements of previous investigators.

Krasovski, in the same year, found the rhamno-xantin from *Rhamnus cathartica* to be identical with the frangulin from *Rhamnus frangula*.

Tutin and Naunton (1914) made an analysis of aloes, finding aloe-emodin and a substance which on hydrolysis yielded aloe emodin and a sugar, but no other anthraquinone derivatives. If his statements are true,—and there seems no very good evidence that they are not, there is reason to wonder just how many non-existent constituents of these anthraquinone containing drugs have been described, and, after all, what effect these substances have on the properties of the drugs.



Summary of analyses, drugs used for tests:

II. Senna. (Analysis by Tutin, 1913) Alexandrian Senna.

Anthraquinone derivatives: Rhein, aloe-emodin, and isorhamnetin, together with glucosides.

Other substances: Essential oil, salicylic acid, kaempferol, kaempferin, the Mg salt of an unidentified organic acid, myricyl alcohol a phytosterol, a phytosterolin, palmitic and stearic acids, chlorophyll, and some amorphous and resinous substances.

Cascara. (Analysis by Jowett, 1904)

Anthraquinone derivatives: emodin and an isomer which melts at 183°, also glucosides yielding on hydrolysis, emodin, chrysophanic acid, rhamnetin.

Other substances: Syringic acid, a fat, rhamnol, rhamnol-arachidate, glucosides of myristic and linolic acids, resins, etc.

(Rhamnol is an alcohol, crystalizing white needles, m.p. 136°).

Rumex. (Tutin, 1910). *Rumex ecklonianus*. (No analyses of *Rumex crispus* are available.)

Anthraquinone derivatives: Chrysophanic acid, emodin, emodin-monomethyl-ester.

Other substances: Essential oil, ceryl alcohol, a phytosterol, probably rhamnol, palmitic and stearic acids, oleic acid, linolic and linolenic acid, ipuranol, traces of other crystalline substances, various resins, and amorphous substances.

Rhubarb: (Analysis by Tutin and Clewer, 1911).

Anthraquinone derivatives: Rhein, emodin, aloe-emodin, emodin-monomethyl-ester, chrysophanic acid, and their glucosides, also rheinolic acid.

Other substances: - - - - -



Cinnamic and gallic acids, dextrose, laevulose, tannin, an amorphous, non-glucosidic resin, a phytosterol, palmitic, stearic, oleic, linolic, linolenic acids, both free and combined, together with resins, etc.

Frangula: No complete analyses of frangula have been made. There seems to be good evidence that it contains emodin and its glucoside, frangulin, possibly also rhein and chrysophanic acid.

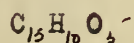
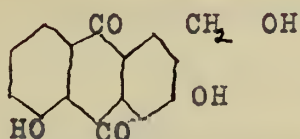
Aloes: (Analysis by Tutin and Naunton, 1914)

Anthraquinone Derivatives: Aloe-emodin and its glucosides.  
Other Constituents: Salicylic acid, a fatty acid, m.p. 75-8, a resin and other amorphous material, which on hydrolysis yielded cinnamic acid, aloe-emodin and a sugar; also a p-coumaric acid.



### III. Summary of Properties : Oxy-anthraquinone Derivatives found in the Drugs Tested.

#### I. Aloe-emodin:



(Robinson and Simonsen's formula, 1910)

Crystallizes in orange red needles, mp. 224'. Soluble in ether, hot alcohol and benzene, soluble dilute ammonia with a red violet color. Soluble con. sulfuric acid and in alkalis with a red color.

Is considered a derivative of  $\alpha$ -methyl anthracene. (From nature of reduction products.)

Separated by precipitating the resins from alcoholic extracts of the drugs containing it, and extracting with ether.

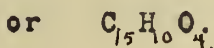
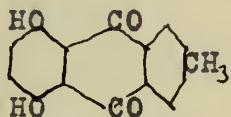
Derivatives probably prepared:

#### I. (a) Chrysamic acid. $C_{14}H_7(NO_2)_4O_4$

Prepared by treating aloes, or emodin with con. nitric acid.

Forms yellow plates or monoclinic prisms. Soluble in alcohol and ether, almost insoluble in water.

#### II. Chrysophanic Acid:



(Jowett and Potter's formula, 1903.)

Crystallizes in golden yellow plates; m.p. 196' when free from emodin-mono-methyl-ester. Insoluble in water and cold solutions of alkali carbonates. Soluble, dilute potassium hydroxide, alcohol, ether, and benzene.



Is considered a derivative of  $\beta$  -methyl anthracene, since it yields  $\beta$  -methyl anthracene on reduction with zinc dust.

Separated by shaking out the ether extract of a drug which contains it with dilute sodium carbonate solution and recrystallizes from ether.

## II. Derivatives probably prepared in course of analysis:

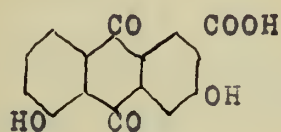
(a) Amino-chrysophanic acid:  $\text{CH}_3 \text{C}_{15}\text{H}_5(\text{OH})\cdot\text{O}_2\text{N H}_2$

Formed on heating chrysophanic acid with concentrated ammonia, to  $200^\circ$ , or on long standing with concentrated ammonia.

(b) Tetra-nitro-chrysophanic acid.  $\text{C}_{15}\text{H}_2(\text{NO}_2)_4\text{O}_4$ .

Formed by warming chrysophanic acid with concentrated nitric acid. Almost insoluble in water.

## III. Rhein.



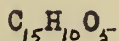
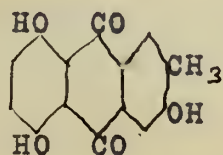
(Robinson and Simonsen's formula, 1909).

Crystallizing in small yellow needles, m.  $321-322^\circ$ .)

Slightly soluble in alcohol, methyl alcohol, acetone, glacial acetic acid, chloroform, ether, benzene, and toluene, soluble in concentrated sulfuric acid, ammonia, and alkalis with a characteristic red color.

May be prepared from aloe-emodin by oxidation with chromic acid.

## IV. Emodin.



(Placing of third OH uncertain.)

(Oesterle's formula, 1911)



Crystallizing red orange needles, m. 250°, crystals lose water at 47°. Soluble in alcohol, amyl alcohol, and acetic acid, less so in benzene. Soluble in ammonia with a red color.

Soluble, concentrated sulfuric acid, alkali hydrates and carbonates, with a characteristic red color.

Yields on zinc dust distillation,  $\beta$ -methyl anthracene.

Prepared by treating the resid from the alcohol extract of the drug with hot toluol, and recrystallizing from glacial acetic acid.

Emodin mono- methyl-ether.

Found closely associated with chrysophanic acid, a fact that accounts for the many melting points given to that substance.

#### V. Glucosides

1. Frangulin:  $C_{21}H_{20}O_9$  = Emodin plus Rhamnose.

Citron yellow, shining needles: m.p. 226°

Insoluble in water and ether, soluble in benzene and warm alcohol, soluble, sulfuric acid and alkalis with red color.

2. Aloin:  $C_{17}H_{14}O_7$ , plus  $1/2$  H<sub>2</sub>O. Aloe-emodin plus (?).

Small, sulfur yellow, prismatic needles; m.p. 147°.

Loses  $1/2$  mol. water at 100°.

Slightly soluble, cold water; soluble, warm water, and alcohol. Soluble in alkali hydrates and carbonates; with orange yellow color. Solutions show green fluorescence. Soluble, water and alcohol; insoluble, benzene, ether, and chloroform. Forms aloetic acid on treatment with fuming nitric acid.



\*\*\* EXPERIMENTAL \*\*\*



- Identification of Drugs Containing Emodin -

I. (a) Preparation of Drug Extracts

The materials, with the exception of the aloes, were obtained from Meyer Bros., St. Louis, in the powder form called for in the U.S.P. formula for fluid extracts; and the fluid extracts were made up according to the directions given in the United States Pharmacopeia; the distillation and evaporation of the alcoholic menstrua being carried out at atmospheric pressure over a steam bath. It may be worth while to state here that the fluid extracts having the weaker alcoholic menstrua, especially Frangula, Rumex, and Senna, showed rather heavy precipitation of a brown resinous substance when allowed to stand several weeks. Senna appears to be more soluble in about two thirds of the amount of menstruum called for by the formula, than in the amount prescribed.

The aloes used was obtained as the resin, and made into a tincture according to the U. S. P. formula except that sawdust in No. 30 powder (which had previously been exhausted with alcohol in strengths varying from 95 to 50%) was substituted for the glycerrhiza.



(b) Objects of Experiments:

The primary object of these experiments was to find a simple method or system of chemical tests by means of which the fluid extracts of these drugs might be distinguished, one from the other. These tests were to be based, if possible, on the action of the different anthraquinone derivatives present, especially their formation of different oxidation and reduction products.

Methods of Procedure:

The tests used were kept as simple as possible; the color reactions of the anthraquinones themselves, and those of the various drugs containing them were tested out for the fluid extracts of the drugs worked with, both in the form described in the literature, and with any modifications made necessary or suggested by circumstances. Besides, the behavior of ether, amyl alcohol, and benzene extracts (made from the fluid extracts of the drugs) toward a system of oxidizing and reducing agents was studied in order to obtain, if possible, derivatives of the anthraquinone products present, which differed enough from one another to give distinctive color tests.

The extracts of the drugs used for testing were, as a rule, made by shaking the fluid extract (1 part) with the solvent (4 parts), allowing the mixture to settle, and separating the solvent later.

The standard color sheets found in Mulliken's "Identification of Pure Organic Compounds." (John Wiley and Sons, New York.) were used in identification of the colors.



## IDENTIFICATION OF DRUGS CONTAINING EMODIN

### Experimental

(For all tests see tables inserted)

II . The first class of tests undertaken were those applied directly to the solutions made by shaking out the fluid extracts with the various solvents, i.e., benzene, amyl alcohol and ether. Of these the following proved the most satisfactory:

1. Shaking the benzene solution with equal parts of concentrated ammonia produces a precipitate with rhubarb, and only a clear red solution with the other drugs. This is probably due to the formation of amino-chrysophanic acid, and is a test which does not seem to be at all known. It holds good in mixtures, even when only a small amount of rhubarb is present.

2. Shaking the amyl alcohol solution with equal parts of concentrated ammonia gives a brilliant yellow-green fluorescence with cascara and aloes, while the other solutions show only the deep red color characteristic of the anthraquinone drugs. There is no mention of this fact in literature, although the test seems to be an important one. Cascara and aloes are easily distinguished from each other, while this is one of the very few good tests which serve to distinguish between cascara and frangula.

3. The amyl alcohol solution of aloes, when treated with a strong solution of mercurous nitrate, turns a brilliant dark red, while the solutions of the other drugs remain colorless. Dragendorff (1872) mentioned the fact that mercurous nitrate turned Barbadoes and Curaco aloes reddish, but there seems to be no mention of the use of this test in later literature.



4. The ether extracts, when treated with solutions of nickel acetate show a rather striking variation in color. Senna develops a dark brilliant red, which becomes violet when treated with KOH; while none of the other solutions become red until treated with alkali, (see tables) when they vary from a dark red to a dark yellow orange; rumex alone being excepted. This drug develops no color with nickel acetate, retaining the green of the nickel salt throughout the test. Numerous writers have mentioned the fact that some emodin compounds give a red color when treated with nickel acetate, but no one seems to have used this reaction as a test to distinguish between drugs containing these compounds. The colors and shades of color developed in this test might serve to distinguish the pure fluid extracts of senna, cascara and aloes. The colors of cascara, frangula and rhubarb are very much alike, but the presence of rhubarb or cascara can very easily be proven by other tests, so this might serve as a test for frangula, if neither of the other two were present.

5. The amyl alcohol solution of aloes when treated with an equal volume of saturated lead subacetate solution, became red while the others remained colorless. This does not seem to have been mentioned, although precipitation tests with lead subacetate are numerous.

Also the benzene solution of rhubarb when treated with lead subacetate gave a yellow orange precipitate which turned red with alkali, while the others gave white precipitates. (See tables).

Other less satisfactory tests applied directly to these solutions were:

1. The iodine test. Several writers mention this as a test for certain varieties of aloes, but it was difficult to see how



the test has been applied. If the iodine in potassium iodine solution were applied directly to the amyl alcohol or benzene solutions, the red violet colors developed were those obtained by treating these solvents with the iodine solution, while treating water or alcohol solutions of the residues from the extracts which had been evaporated on the water bath gave only a more or less reddish color, according to the solvent and the amount of iodine used. The test, therefore, seems to be worthless.

2. The borax solution test. Schoutelen, (1893) stated that concentrated borax solutions produced, on standing from twenty to twenty-five minutes with solutions containing aloes 1-10000, a yellow green fluorescence. This reagent was tested with the various solutions of aloes, and with water solutions of the residues left when the solutions were evaporated; together with alcohol solutions of these residues. The only solutions which gave decided fluorescence were the water and alcohol solutions of the ether residues, although there was some fluorescence in the alcohol solution of the resins precipitated by pouring the tincture of aloes into a large excess of water, as well as in the water solution of the aloes itself. The duplicate solutions of the ether residues from cascara and rumex were light orange red, while those from senna, rhubarb, frangula, and aloes were red, the aloes being the darkest shade.



# Explanation of Terms used in Tables:

Colors, unless preceded by the mark "B.T." are those of sheets C. and D. Those marked "B.T." indicate the colors on sheet E.; i.e. "Broken Tones."

The concentrated ammonia and also the acids used are the ordinary laboratory reagents.  $\text{SnCl}_2$  solution was made by saturating distilled water at room temperature with crystals of stannous chloride, and adding about four drops of concentrated hydrochloric acid to 100 cc solution. The nickel acetate solution was likewise saturated at room temperature.

Strong solutions of most of the reagents used have been found to give better results than weak solutions.



Benzene Solutions.

5 cc Solution,  
5 cc  $\text{NH}_4\text{OH}$ ,

5 cc solution,  
5 cc  $\text{HgNO}_3$ ,

5 cc solution,  
5 cc  $\text{NiAc}$ .

Senna.

Upper layer,  
orange-yellow.

Does not  
appreciably  
change color.

Lower layer,  
orange,  
shade 1.

Lower layer,  
red, tint 1.

Solution  
clear.

Cascara.

Upper layer,  
orange-yellow,  
shade 2.

"

Does not change  
color.

Lower layer,  
orange-red, sh1,

Rumex.

Upper layer,  
n. orange-  
yellow.  
Lower layer,  
red, tint 1.

"

"

Rhubarb.

Upper layer,  
orange-yellow,  
Lower layer,  
red, sh. 1.  
Prec. violet-  
red, tint 2.

"

Lower Layer,  
red-orange,  
shade 2.  
Solution  
muddy.

Frangula.

Upper layer,  
orange, sh. 1.  
Lower layer,  
violet-red,  
tint 1.

"

Lower layer,  
red-orange,  
shade 2.  
to yellow.

Aloes.

Upper layer,  
orange-yellow,  
Lower layer,  
yellow.

"

Does not  
change color.



Benzene Solutions, II.

	5 cc solution, 5 cc NiAc. KOH to alkalinity.	5 cc solution, 5 cc sat. PbOAc.	Same, KOH to alkalinity.
Senna.	Prec. med. violet. Sol. light orange-red. Benzene layer, colorless.	Lower layer, yellow-orange, tint 2. (light) Upper layer does not change color.	Color of clear solution. Red, tint 2. Prec. white.
Cascara.	Prec. red, shade 2. Contact layer, red. Benzene layer, colorless.	Lower layer, colorless. Upper layer, does not change color.	Sol. after settling. red, tint 1. Prec. white.
Rumex.	Prec dark blue- green to violet. Contact layer, red. Benzene layer colorless.	"	Sol. after settling, orange-red, tint 2. Prec. white.
Rhubarb.	Prec. violet-red, shade 2. Contact layer, red, shade 2. Benzene layer, red, shade 2.	Lower layer, prec. yellow- orange, sh. 1. Upper layer, orange, sh. 1.	Sol. after settling, red, shade 1. Prec. red.
Frangula.	Prec. dark red-violet. Sol. clear and colorless.	No change in colors.	Sol. after settling, red, tint 1. Prec. white.
Aloes.	Prec. blue-green to violet. Sol. clear and colorless.		Sol. after settling, orange-red, tint 2. Prec. white.



Amyl Alcohol Solutions.

5 cc solution,  
5 cc sat  $\text{HgNO}_3$ ,

5 cc solution,  
5 cc con  $\text{NH}_4\text{OH}$ ,

5 cc solution,  
5 cc sat.  $\text{NiAC}$ .

Senna.

Solution does  
not change  
color.

Normal red-  
orange.

Lower layer,  
red-orange,  
normal to  
tint 1.

Cascara.

"

Normal or.-red  
by transmitted  
light,  
Dark yellow-  
green  
fluorescence.

Lower layer,  
orange-yellow,  
shade 2  
Upper layer,  
muddy.

Rumex.

"

Normal  
yellow-orange.

Lower layer,  
light green,  
Upper layer,  
yellow,  
shade 1.

Rhubarb.

"

Normal  
red-orange.

Lower layer,  
yellow-orange,  
shade 1.  
No change in  
upper layer.

Frangula.

"

Normal  
orange-red,

No appreciable  
change in  
color.

Aloes.

Lower layer,  
Deep red.

Normal-orange-  
red, transmitted  
light,  
Yellow-green  
fluorescence.

Lower layer  
yellow-orange  
to orange.



Amyl Alcohol Solutions, II.

	5 cc solution, 5 cc sat. NiAc, (colors after shaking)	5 cc solution, 5 cc PbOAc. sol.	5 cc EtOH sol. Amyl alcohol residue. PbOAc & KOH.
Senna.	Orange, shade 1,	Lower and upper layers clear, Prec at point of contact, orange-yellow, shade 1.	Sol. almost colorless, trace red.
Cascara.	Normal red.	Prec. darker, otherwise like senna.	Solution, yellow-orange, shade 1.
Rumex.	Yellow-orange, shade 2.	Like Senna.	Solution almost color- less, trace red.
Rhubarb.	Orange, shade 1.	Like senna.	Solution red, tint 2.
Frangula.	Red, tint 1.	Like senna.	Solution red, tint 2.
Aloes.	Yellow-orange, shade 2, to black.	Lower layer, normal red.	Yellow-orange, shade 1.



Ether Solutions.

5 cc solution,  
5 cc con.  $\text{NH}_4\text{OH}$ ,

5 cc solution,  
5 cc  $\text{HgNO}_3$   
sat. sol.

5 cc solution,  
5 cc sat.  $\text{NiAc}$   
(colors three  
minutes after  
adding.)

Senna.

Violet-red,  
tint 1,  
(clear)

No change.

Lower layer,  
red, shade 1.

Cascara.

Orange-red,  
shade 2,  
(upper layer  
cloudy)

"

Lower layer,  
yellow,  
shade 1,

Rumex.

Orange,  
shade 1,  
Upper layer  
lighter.

"

Lower layer,  
clear green,  
shade 1.

Rhubarb.

Normal  
orange-red.

"

Lower layer,  
orange,  
shade 2,

Frangula.

Normal  
orange-red,

"

Lower layer,  
yellow-orange,  
shade 2.

Aloes.

Orange,  
shade 1.  
(upper layer  
lighter)

"

Lower layer,  
green,  
shade 2.  
(much darker.



## Ether Solutions II.

	5 cc solution, 5 cc NiAc, KOH to alkalinity.	5 cc solution, 5 cc PbOAc sol.	Same, KOH to alk. (Colors after the prec. has settled.)
Senna.	Prec. violet, tint 1. Ether layer uncolored.	Prec. orange, shade 1.	Lower layer, red-orange, tint 1.
Cascara.	Prec. dark orange-red, Ether layer uncolored.	Prec. orange-yellow, shade 2.	Lower layer, orange-red, tint 1.
Rumex.	Prec. med. green. Ether layer uncolored.	Prec. yellow-orange, shade 1.	Lower layer, orange, tint 1.
Rhubarb.	Prec. dark red-violet, Ether layer, red.	Prec. orange-yellow, shade 2.	Lower layer, orange-red, tint 1. Ether layer N. red-orange.
Frangula.	Prec. dark red-violet, Ether layer uncolored.	Prec. orange-yellow, shade 2.	Lower layer, orange-red, tint 1.
Aloes.	Prec. Med. greenish- yellow to dark yellow.	Prec. yellow-orange, shade 2. Solution the only one colored.	Lower layer, orange.



### III. Tests applied to the residues left after evaporating solutions of the drugs.

1. Oxidation and reduction tests with nitric acid and stannous chloride.

2 cc portions of the different solutions were evaporated, and the residues taken up with 1 cc. concentrated nitric acid; and again evaporated; the residues varying in color from yellow to red-brown. Rumex and senna were always lighter in color than the others, and the solution of aloes in benzene gave a much lighter residue than the solutions of the same drug in other solvents.

When these residues were treated with a saturated solution of stannous chloride containing a few drops of hydrochloric acid, the residues from the benzene and ether solutions of senna turned green, those from aloes, yellowish brown, and the others from red to red-violet, the color of the rumex residue being lightest.

Like tests were made with the residues left after treating the ether solutions with nitric acid, using ferrous sulfate, instead of stannous chloride, but these were not at all satisfactory, because of the effect of the color of the iron salts.

Other reduction tests were made, also, using formaldehyde, etc, but stannous chloride was the only effective reducing agent found.

An effort was made to diazotize the compounds so formed by treating with sodium nitrite solution in ice water; the nature of the compound thus obtained being judged by the color or the depth of color it gave when treated with alkalies. Although the degree of difference between the colors of the compounds



formed in this way was great enough to distinguish between the fluid extracts of the pure drugs, the tests were not entirely satisfactory in mixtures.

It seems evident that compounds of different nature are formed by the reduction of drugs containing aloe-emodin and frangula-emodin; the more or less deep red-violet color which characterizes the solutions of the drugs containing frangula-emodin differs so markedly from the greens and browns of senna and aloes.



Resids from 3 cc Ether Solutions.

1 cc  $\text{HNO}_3$ ,

1 cc  $\text{HNO}_3$ ,  
 $\text{SnCl}_2$  sol. to  
cover dry  
resid.

Same,  $\text{SnCl}_2$   
decanted,  
resid washed,  
 $\text{H}_2\text{O}$ , dissolved  
10 cc alcohol.

Senna.

Orange-yellow,  
shade 1.

Greenish-yellow,  
med. to  
yellow-green,  
shade 1.

Greenish-  
yellow to  
yellowgreen,  
shade 1.

Cascara.

Orange,  
shade 2.

Practically  
black,  
orange-yellow  
al edges.

B.T.  
Med. red.

Rumex.

Orange,  
shade 1.

B.T.  
Dark red-  
violet.

Violet-red,  
tint 1.

Rhubarb.

Orange,  
shade 2.

B.T.  
Dark red-  
violet.

Red-violet,  
shade 1.

Frangula.

Orange,  
shade 2.

B.T.  
Dark red-  
violet.

Red, tint 1.

Aloes.

Red-orange,  
shade 2.  
(Colored  
immediately.)

Red-orange,  
shade 2.  
(Darker than  
chart)

Orange,  
shade 2.



Resids from 3 cc Ether Solutions.

1 cc  $\text{HNO}_3$ , evap.  
reduced,  $\text{SnCl}_2$

1 cc  $\text{HNO}_3$ , evap.  
1 cc  $\text{FeSO}_4$  sol.  
alkaline,  $\text{KOH}$ .

1 cc  $\text{HNO}_3$ , evap.  
2 cc  $\text{FeSO}_4$  sol.  
washed,  $\text{H}_2\text{O}$ ,  
10 cc  $\text{EtOH}$ ,  
 $\text{KOH}$  till  
alkaline.

Senna.

Red-tint 1.  
(alcohol and  
water sols  
check.)

B.T.  
Yellow-orange,  
shade 2.

Orange-yellow,  
shade 2.

Cascara.

Red-orange,  
shade 2.

B.T.  
Yellow,  
shade 2.

Orange-red,  
shade 2.

Rumex.

Orange-yellow,  
shade 2.

Yellow,  
shade 2.

Yellow-orange,  
shade 2.

Rhubarb.

Alcohol sol.  
B.T. med. orange.

Yellow,  
shade 2.

Yellow-orange,  
shade 1.

Water sol.  
B.T. med. red.

Frangula.

Yellow-orange,  
shade 2.  
(alcohol and  
water solutions  
check)

yellow,  
shade 2.

Orange-red,  
shade 2.

Aloes.

B.T.  
Darkest  
red-orange.

Orange,  
shade 2.

Black.



Resids from 3 cc amyl alcohol solutions.

HNO<sub>3</sub>, 1cc.

HNO<sub>3</sub> 1 cc evap.  
sol<sub>2</sub> to cover  
resid.

same,  
washed, H<sub>2</sub>O,  
2 cc sat.  
w/ NO<sub>2</sub> sol.

Senna.

orange-yellow,  
shade 1.

resid, darkest  
gray.

violet-red,  
tint 2.  
(very light)

alcohol solution,  
warm dark gray.

Cascara.

orange,  
shade 2.

B.T.  
Light red.

med.  
yellow orange.

resid brownish to  
red.

Rumex.

orange,  
shade 1.

Sol.  
Almost colorless,  
red-violet tint.  
resid.  
yellow orange,  
violet at edges.

Almost colorless

Rhubarb.

Orange,  
shade 1.

Sol.  
B.T. light  
red violet.

Light  
orange-red,  
tint 9.

resid,  
dark red-  
violet.

Frangula.

orange,  
shade 1.

Sol.  
violet-red,  
tint 2.

Almost colorless

resid,  
dark red-violet.

Aloes.

N. orange-red.

Sol.  
B.T. Med.  
orange.

Red-orange,  
shade 2.  
(very dark)

resid,  
dark red-orange.



Resids from 3 cc Benzene solutions.

1 cc  $\text{HNO}_3$ , evap.  
10 cc alcohol.

1 cc  $\text{HNO}_3$ , evap.  
2 cc sat.  $\text{SnCl}_2$   
(colors of  
resids)

1 cc  $\text{HNO}_3$ , evap  
Red.  $\text{SnCl}_2$ ,  
washed,  $\text{H}_2\text{O}$ .  
dissolved,  
10 cc, EtOH.

Senna.

Normal  
orange-yellow.

B.T.  
med. to dark  
greenish  
yellow.

Light  
greenish  
yellow.

Cascara.

Normal  
orange-red.

Red, shade 2.  
(very dark)

Med. yellow-  
orange.  
Resid very  
slightly  
soluble.

Rumex.

Orange,  
shade 1.

Violet-red,  
shade 1.

Light red-  
violet.  
Asked, if  
entire resid  
is not nitrated  
and reduced.

Rhubarb.

Normal  
orange-yellow.

B.T.  
red-violet.  
(darker than  
chart)

Red, shade 2.  
very dark.

Frangula.

Orange-yellow,  
shade 1.  
(light)

Violet-red,  
shade 2.

Red, tint 1.  
Asked, if entire  
resid is not  
nitrated and  
reduced.

Aloes.

Orange-yellow,  
shade 1.

Dark yellow.

Neutral gray  
to colorless.



## Resids from 3 cc Benzene Solutions.

	1 cc HNO <sub>3</sub> . evap. SnCl <sub>2</sub> to resid, Dissolved, 10 cc ETOH. treated, NaNO <sub>2</sub> in ice- water.	Same, Made alkaline, KOH.	1 cc HNO <sub>3</sub> . SnCl <sub>2</sub> to resid Cl water, 4 cc KOH till alkaline.
Senna.	B.T. Light greenish- yellow sol.  White prec.	led, tint 2.	Orange-red, tint 1.
Cascara.	Dark yellow- orange sol.  Prec. dark neutral gray.	Violet-red, shade 1.	B.T. Violet-red, tint 1. (nearer red than chart)
Rumex.	B.T.  Light-red violet sol.  White prec.	B.T. Light red- violet.	B.T. Med. red.
Rhubarb.	B.T. Black sol.  Prec. dark neutral gray.	B.T. Med. red.	Red, shade 2.
Frangula.	B.T. Light red- orange sol.  Muddy, but no precipitation.	B.T. Med. red.	Normal orange-red.
Aloes.	Prec. greenish- yellow to yellow green.	med. yellow-orange.	Med. yellow-orange



2. An effort was made to obtain nitration products other than those formed by the evaporation with nitric acid; (a) by treating the residues left after evaporating the solutions of the drugs with one part nitric and one-half part sulfuric acid, heating to the temperature of the steam bath, and partially neutralizing the product so obtained with sodium or barium carbonates. It was very noticeable that the red orange solutions of cascara and frangula became deeper and darker in color with the carbonates; those of rhubarb were only a little less red, while those of the others varied from yellow to yellow orange. Reduction with stannous chloride produced a red with cascara and frangula, and colors varying from yellow to orange with the others. Aside from these reactions this series of tests were not so satisfactory as the one with the nitric acid alone, for the sodium and barium salts precipitated and interfered with the following operations. (See tables.)

3. Attempts were made to synthesize dye-stuffs by treating the diazotized residues from the stannous chloride reductions with organic bases, e.g., aniline, dimethyl-aniline, pyridine, etc.; but, while some very brilliant reds and greens were obtained, especially with dimethyl aniline, the colors of all the solutions were alike; and it was impossible to tell to what extent the dye-stuffs obtained were combinations of the reagents employed.



	Resids from 3 cc	Ether Solutions.	
	$1\text{ cc HNO}_3,$ $1/2\text{ cc H}_2\text{SO}_4,$ $5\text{ cc sat. Na}_2\text{CO}_3$ (sol. acid.)	$1\text{ cc HNO}_3,$ $1/2\text{ cc H}_2\text{SO}_4,$ $5\text{ cc sat Na}_2\text{CO}_3,$ $2\text{ cc SnCl}_2\text{ sol.}$	$1\text{ cc HNO}_3,$ $1/2\text{ cc H}_2\text{SO}_4,$ Neut. $\text{Na}_2\text{CO}_3$ Acid, $\text{HCl},$ $2\text{ cc SnCl}_2\text{ sol.}$ KOH to ALK.
Senna.	Yellow, tint 1.	B.T. Med. orange-red.	Red, tint 1.
Cascara.	Orange, normal tone.	B.T. Dark red.	Red-orange, shade 2.
Rumex.	Yellow-orange, tint 1.	Med. yellow- orange.	Orange-yellow, shade 2.
Rhubarb.	Normal orange-yellow.	Violet-red. Shade 1.	Yellow-orange, shade 2.
Frangula.	Red-orange, normal tone.	Violet-red, shade 2.	Yellow-orange, shade 2.
Aloes.	Orange-yellow, shade 1.	Orange, shade 2.	Red-orange, shade 2.



Resids from 3 cc Ether Solutions.

1 cc  $\text{HNO}_3$ ,  
 $\text{Na}_2\text{CO}_3$ , alkaline.

1 cc  $\text{HNO}_3$ , evap.  
 10 cc alcohol,  
 $\text{Na}_2\text{CO}_3$ ,

1 cc  $\text{HNO}_3$ , evap.  
 10 cc alcohol,  
 $\text{Na}_2\text{CO}_3$ ,  
 $\text{SnCl}_2$ , reduction

Senna.

Red, tint 1.

Red, tint 1.

B.T.  
 Light yellow.

Cascara.

Orange,  
 shade 1.

Red-orange,  
 shade 2.  
 (darker)

B.T.  
 Dark red-  
 violet .

Rumex.

Yellow-orange,  
 Dark.

B.T.  
 Med. orange.

B.T.  
 Dark  
 yellow-orange.  
 Lighter than  
 chart.

Rhubarb.

B.T.  
 Dark yellow-  
 orange.

Orange-red,  
 shade 2.

B.T.  
 Yellow-orange.  
 (dark)

Frangula.

Violet-red.  
 shade 2.

Orange-red,  
 shade 2.

B.T.  
 Yellow-orange,  
 Dark.

Aloes.

Red-orange,  
 shade 2.

Red, shade 2.

Red, shade 2.



Resids from 3 cc Ether Solutions.

1 cc  $\text{HNO}_3$ ,  
5 cc  $\text{H}_2\text{O}$ .  
 $\text{BaCCl}_2$  to  
neutrality.

1 cc  $\text{HNO}_3$ ,  
 $1/2$  cc  $\text{H}_2\text{SO}_4$ ,  
10 cc  $\text{H}_2\text{O}$ ,  
 $\text{BaCO}_3$ , acid.

Senna.	Normal yellow-orange.	Greenish-yellow tint 2.
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Cascara.	B.T. Dark orange.	Normal orange. whole solution.
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Rumex.	Orange-yellow, shade 2.	Orange-yellow, tint 2.
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Rhubarb.	Yellow-orange, shade 1.	Orange-yellow, tint 2.
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Frangula.	Orange-yellow, shade 2.	Normal red- orange, (whole sol.)
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Aloes.	B.T. Dark orange.	Yellow, tint 2.
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Amyl Alcohol Solutions.

3 cc Resid.  
1 cc  $\text{HNO}_3$ ,  
 $1/2$  cc  $\text{H}_2\text{SO}_4$ ,  
10 cc sat.  $\text{Na}_2\text{CO}_3$

3 cc Resid.,  
1 cc  $\text{HNO}_3$ ,  
 $1/2$  cc  $\text{H}_2\text{SO}_4$ ,  
5 cc sat.  $\text{Na}_2\text{CO}_3$

5 cc resid.,  
1 cc  $\text{HNO}_3$ ,  
 $1/2$  cc  $\text{H}_2\text{SO}_4$ ,  
5.612 cc  $\text{Na}_2\text{CO}_3$   
2 cc sat  $\text{SnCl}_2$

Senna.

Normal  
orange -yellow.

Normal  
orange-yellow.

Colors vary  
hardly at all.  
Red to  
yellow-orange.

Cascara.

Orange,  
shade 1.

Solution.  
Orange,  
shade 1.  
Prec.  
orange, shade 1.

"

Rumex.

Yellow-orange,  
shade 1.

Normal  
yellow-orange,  
No precipitate.

"

Rhubarb.

Red-orange,  
shade 1.

Yellow-orange.  
(lighter and  
duller than  
normal)  
No prec.

"

Frangula.

Orange,  
shade 1.

Yellow-orange,  
(Dye-stuff like  
prec. on dish,  
Normal-red)

"

Aloes.

Orange,  
shade 1.

Yellow-orange,  
shade 1.  
Prec.  
Yellow-orange,  
shade 2.

"



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Resids from 3 cc Amyl Alcohol Solutions.

2 cc Sn Cl red.  
of  $H_2SO_4$  &  $HNO_3$   
solutions,  
treated both  
strengths  
 $Na_2CO_3$  solutions.  
 $Na NO_2$ , 2 cc.

Senna.

Sol.  
red-orange,  
shade 1.

Cascara.

Prec. on foam,  
orange, sh. 1.

Sol. orange,  
shade 2.

Rumex.

Yellow-orange,  
shade 2.

Foam light.

Rhubarb.

B.T.  
Light  
yelloworange.

Foam light.

Frangula.

Orange,  
tint 1.

Aloes.

Foam orange,  
shade 2.  
Solution a  
darker shade.



Resids from 3 cc Benzene Solutions.

1 cc  $\text{HNO}_3$ .  
 $1/2$  cc  $\text{H}_2\text{SO}_4$ ,  
 5 cc sat.  
 $\text{Na}_2\text{CO}_3$  sol.

1 cc  $\text{HNO}_3$ .  
 $1/2$  cc  $\text{H}_2\text{SO}_4$ ,  
 $\text{Na}_2\text{CO}_3$  to  
 neutrality.

1 cc  $\text{HNO}_3$ .  
 $1/2$  cc  $\text{H}_2\text{SO}_4$ ,  
 5 cc sat.  
 $\text{Na}_2\text{CO}_3$  sol.

Senna.

Yellow,  
 shade 1.  
 (light)

Red, tint 1.

Yellow,  
 tint 1.

Cascara.

Normal  
 red-orange.

Orange-red,  
 shade 2.  
 (neutral, 10 cc  
 $\text{Na}_2\text{CO}_3$  sol.)

Sol.  
 red, shade 2.  
 Prec. violet-  
 red, shade 2.

Rumex.

Yellow-orange,  
 tint 1.

Yellow-orange,  
 tint 1.

B.T.  
 Light red.

Rhubarb.

N. orange-red.  
 Dye-stuff like  
 prec.  
 normal red.

Red, shade 2.

Sol. red-  
 orange, sh. 2.  
 Prec. dark  
 red-orange.

Frangula.

Normal red-  
 orange.

B.T.  
 Med. orange.

Sol. B.T.  
 red. orange-red  
 Prec. dark  
 red-violet.

Aloes.

Normal orange-  
 yellow.

Red-orange.

Yellow-  
 orange, shade 2



Resids from 3 cc Benzene Solutions.

1 cc  $\text{HNO}_3$ ,  
 $1/2$   $\text{H}_2\text{SO}_4$ ,  
 5 cc  $\text{Na}_2\text{CO}_3$ ,  
 2 cc  $\text{Sn Cl}_2$ ,  
 2 cc  $\text{Na NO}_2$ ,  
 KOH. alkaline.

1 cc  $\text{HNO}_3$ ,  
 1 cc  $\text{H}_2\text{SO}_4$ ,  
 5 cc  $\text{Na}_2\text{CO}_3$ ,  
 2 cc  $\text{Sn Cl}_2$ ,  
 2 cc  $\text{Na NO}_2$ ,

Same, except  
 except 10 cc  
 or more  $\text{Na}_2\text{CO}_3$   
 slightly acid  
 before adding  
 $\text{Sn Cl}_2$ .

Senna.

Normal  
 red-violet.

Light  
 yellow-orange.

Normal  
 red-violet.

Prec.  
 same color.

Prec. same  
 color.

Cascara.

B.T.  
 Violet-blue,  
 shade 2.

B.T.  
 mod. red.

B.T.  
 Dark red-violet.  
 Dilutes  
 violet-red.

Dilutes  
 violet-blue.

Rumex.

B. T.  
 Dark blue-  
 violet.

B.T.  
 light yellow-  
 orange.

B.T.  
 Dark red-violet,  
 Dilutes  
 red-violet.

Rhubarb.

Violet-red,  
 shade 2.  
 Dilutes  
 N. violet red.

B.T.  
 dark red-orange.

Violet-red,  
 shade 2.  
 Darker than  
 chart.

Frangula.

Violet-blue,  
 shade 2.  
 Dilutes  
 violet-blue.

B.T.  
 light red.

Violet-red,  
 shade 2.  
 Dilutes  
 violet red.

Aloes.

Dark  
 green gray.

B.T.  
 yellow-orange.

B.T.  
 red-red.  
 Dilutes  
 light red.



Resids from 3 cc Benzene Solutions.

1 cc  $\text{HNO}_3$ ,  
1/2 cc  $\text{H}_2\text{SO}_4$ .  
 $\text{BaCO}_3$ , acid.  
solution.

1 cc  $\text{HNO}_3$ ,  
Evap.  
Treated with  
 $\text{Ba}(\text{OH})_2$  sol.

1 cc.  $\text{HNO}_3$   
Evap. dissolved  
EtOH, 10 cc.  
 $\text{Ba}(\text{OH})_2$  5 cc  
sat. sol.

Senna.

Yellow, tint 1.  
White Prec.

Violet-red,  
tint 1.  
  
(almost insol.  
EtOH, sl.  
violet tint)

Red, tint 1.  
(slightly  
violet)

Cascara.

Red-orange,  
tint 1.  
  
Orange Prec.

Violet-red,  
shade 2.  
  
EtOH sol.  
red, tint 1.

Orange-red,  
shade 2.

Rumex.

Orange-yellow,  
tint 2.  
  
White prec.

Violet-red,  
tint 2.  
  
(almost insol.  
EtOH)

Orange,  
shade 1.

Rhubarb.

Normal orange.  
Yellow-orange  
precipitate.

Violet-red,  
shade 1.  
  
Alcohol sol.  
yellow-orange,  
shade 2.

Red  
shade 1.

Frangula.

Orange, tint 1.  
  
Orange prec.

Violet-red,  
shade 2.  
(almost insol.  
alcohol, sol  
yellow)

Red-orange,  
shade 2.

Aloes.

Yellow, tint 1.  
  
Prec. white.

Orange-yellow,  
shade 2.  
EtOH sol.  
orange-red,  
shade 2.

Orange,  
shade 1.



Resids from 3 cc Amyl Alcohol Solutions.

1 cc  $\text{HNO}_3$ , evap.  
10 cc EtOH.

1 cc  $\text{HNO}_3$ , evap.  
10 cc EtOH,  
10 cc sat.  
 $\text{Ba}(\text{OH})_2$  sol.

Senna.

Orange,  
shade 2.

Red-orange,  
shade 1.

Cascara.

Orange,  
shade 2.

Darkest brown  
to black.

Rumex.

Orange,  
shade 1.  
(lighter)

Yellow-orange,  
shade 2.

Rhubarb.

Orange,  
shade 1.  
(lighter)

Orange-red,  
shade 1.

Frangula.

Normal  
orange-red.

Yellow-orange,  
shade 2.

Aloes.

Orange,  
shade 2.

Darkest brown  
to black.



3. The effect of chlorine water and sodium hypochlorite as oxidizing agents on the residues from the stannous chloride reductions was tested, and it was found that the formation of the typical red violet color with alkalies was affected to a different degree with different drugs, a fact that was, probably, due to the different anthraquinone-derivatives being oxidized with different degrees of ease, and also to the formation of different intermediate oxidation products; and different concentrations, the last factor being the most important. It was soon evident, however, that the exact control of conditions of temperature, and of the concentration of solutions which was necessary to obtain check results, as well as the slight amount of actual difference between the colors, made the tests impracticable as means of distinguishing between the commercial fluid extracts of these drugs. These reasons led, also, to the abandonment of a series of color tests of similar nature, using copper sulfate, or nickel acetate and chlorine water. (For results of the best of these tests see tables under ether solutions.)

The potassium cyanide test for aloes, which consisted in treatment of the residue from a drug solution with potassium cyanide in potassium hydroxide solution was tried, and found to give a red color with all the drugs tested. This seems to be a good general reaction for this group of drugs.

With the exception of this last reaction, none of these solution residue tests are mentioned in literature.



Resids from 3 cc Ether Solutions.

Diss. 19 cc EtOH  
4 cc Cl water,  
1 drop sat. NiAc,  
2 drops sat. KOH.

Dissolved,  
10 cc EtOH,  
1 drop sat.  
NiAc sol.

Same,  
4 cc Cl water,  
10 drops  
con. HCl,  
KOH to  
alkalinity.

Senna.

Clear solution,  
red, tint 2.  
Prec. flaky and  
cryst. in app.  
N violet-red.

Normal red.  
Soluble,  
slight prec.

Sol.  
red, tint 1.  
Prec.  
N. violet-red.

Cascara.

Red, shade 1.  
Sol. muddy.

Normal  
orange-red.  
Soluble.

Red, tint 2.

Rumex.

Orange, shade 1.  
Sol. cloudy.

Yellow-orange,  
shade 1.  
Sol. cloudy.

Orange,  
shade 1.

Rhubarb.

Sol. muddy,  
red, shade 1.  
Prec.  
Dark brown.

N. orange-red,  
Soluble.

Red, tint 1.

Frangula.

Red, shade 1.  
Sol. muddy.

Normal red.

Violet-red,  
shade 1.

Aloes.

Brown black.

Yellow-orange,  
shade 2.

Yellow-orange,  
shade 2.



## Resids from 3 cc Ether Solutions.

1 cc  $\text{HNO}_3$ , evap.  
 2 cc  $\text{SnCl}_2$ ,  
 washed,  $\text{H}_2\text{O}$ ,  
 5 cc U.S.P.  
 Cl water,  
 alkeline, KOH.

2 cc U.S.P.  
 Cl water,  
 4 drops sat. KOH

1 cc  $\text{HNO}_3$ , evap.  
 10 cc EtOH,  
 3 drops KCN sol.

Senna.

Colorless.

Red, tint 1.

Red, tint 1.  
 (clear)

Cascara.

Dark red.

Red, shade 1.

Orange-red,  
 shade 1.  
 (Heavy, flocc.  
 black prec.)

Rumex.

Colorless.

Orange-red,  
 tint 1.

Red-orange,  
 shade 1.  
 (Light prec)

Rhubarb.

B.T.  
 Light greenish-  
 yellow.

Red, shade 1.

Red, shade 1.  
 (Light prec.)

Frangula.

B.T.  
 Med. greenish-  
 yellow.

Orange-red,  
 shade 1.

Orange-red,  
 shade 1.  
 (Light prec.)

Aloes.

Black brown.

Orange-yellow,  
 shade 2.

Orange,  
 shade 2.  
 (Light prec.)



IV. Tests applied to the resins precipitated by pouring the fluid extracts of the drugs into a large excess of water:

1. Alvarez's sodium peroxide test.

Alvarez 1907, stated that if emodin (1 g.) were treated with sodium peroxide, (0.1 to 3 g,) and 5 cc alcohol in a porcelain capsule, to which was added, after four to five minutes, 10 cc. water, a red color would be developed in the aqueous solution. Using this method of procedure, the resins of the various drugs were treated with sodium peroxide, alcohol, and water. Rhubarb gave a red solution with alcohol, and normal orange-red with water; senna and aloes, colorless, with alcohol, and yellow-orange and orange-yellow, respectively, with water; cascara and rumex were colorless in alcohol solution and orange in water solution, while frangula was colorless and orange red.

2. Sublimation tests:

Rosenthaler (1911) published a series of sublimation tests for drugs which he applied to senna, cascara, and rhubarb. His original paper was not available, and his method for carrying out the tests had to be judged from very brief abstracts. Consequently it is possible that the method used in making the sublimate was not the one he used. The drugs, both in the original powder forms, and as the resins described above, were placed in the bottoms of hard glass test tubes; pains being taken to allow none of the powder to adhere to the sides of the test tubes. These were connected to side-arm test tubes by glass tubing fitted into rubber stoppers; and the side arms of the test tubes were, in turn, connected to the suction pump. The ends of the tubes containing the drugs were then heated in



a sulfuric acid bath to 250° C.

The powdered drugs and the resins gave, essentially, the same sublimates when the resins had been completely dried. A third series, however, which were carried through in open test tubes either gave no characteristic sublimates, or none at all.

The sublimates obtained did not answer exactly to Rosenthaler's description, and while it is probable that he did not use the same varieties of drugs for his tests, the evidence seems to be that the tests are rather less easily applied to obtain reliable results than is generally considered.

The following is a list of results obtained:

Senna. - Amorphous or resinous yellow sublimate, containing masses of a darker color. Brownish with ferric chloride, red with sodium hydroxide, shows no crystals under the microscope. Becomes dark with  $\text{FeCl}_3$ .

Cascara: Sublimate yellow and resinous. No crystals under the microscope. Contains masses of a darker yellow. Darkens with  $\text{FeCl}_3$ .

Rumex: One sublimate showed a leaf and branch formation, but it could not be duplicated. Consisted, for the most part, of a yellow resin containing masses of a darker color. Alcohol solution of the sublimate becomes dark with  $\text{FeCl}_3$ . and red with  $\text{KOH}$ .

Rhubarb: Sublimate normal yellow; mostly amorphous, but showing tiny clusters of radiating crystals under low power, like those of dextrosazone. The sublimate from the resin in this case, was not so satisfactory, as that from the powder. Becomes dark with  $\text{FeCl}_3$ .

Frangula: Sublimate on standing forms in clusters of



needles or columns, appearing to the naked eye as well formed crystals, but appearing less well formed under the microscope.

Brownish to brownish black with  $\text{FeCl}_3$ .

Aloes does not give a sublimate.



\*\*\* RESULTS OBTAINED \*\*\*



## Identification of Drugs Containing Emodin

### I. Summary: Tests for Different Drugs.

#### I. General tests:

1. Red colors of the solutions and residues from solutions with concentrated ammonia and fixed alkalies.
2. Red colors of the nitric acid residues when treated with KCN in KOH solution.
3. Reddish or orange colors of the different residues with nitric and sulfuric acids.

#### II. Tests for Senna.

1. The ether solution when treated with an equal amount of nickel acetate (saturated solution) becomes a deep red, while the others vary from green to orange brown. When treated with KOH the senna solution forms a violet precipitate, while the soluble part of the solution returns to the color of the original ether solution of senna.

2. If 2 cc. of the ether solutions are evaporated, treated with 1 cc. of nitric acid and again evaporated, and the residues so obtained are treated with one or two cc. of a saturated solution of  $\text{SnCl}_2$ ; senna gives a green resid; aloes a brown one, and the rest are red violet. The benzene solution of senna gives the same reaction, but the amyl alcohol solution does not.

3. The diazotized solutions of senna are either red tints, or nearer red than the other solutions treated the same way. The light red or pink color of senna solutions is harder to destroy by adding an excess of chlorine water than the deeper reds of the drugs containing frangula emodin.



### III. Tests for Cascara:

1. The amyl alcohol solution of a fluid extract of cascara, made after shaking it with benzene, gives a green fluorescence when treated with ammonia. Aloes also reacts in this way, but may easily be detected by other color tests. If aloes is found to be present by these tests the presence of cascara may be confirmed or disproved by evaporating a small part of the benzene solution of the drug to be tested, taking up with nitric acid, evaporating again, and reducing with  $\text{SnCl}_2$ , when the aloes residue is yellow, and that from cascara deep red.

2. Cascara, frangula, and to a less extent rhubarb residues from benzene solutions, when treated with nitric acid (one part) and sulfuric acid ( $1/2$  part) and a smaller amount of sodium or barium carbonates than is necessary to neutralize the acid present are orange red while the other solutions develop little or no color.

### IV. Rumex.

1. The ether extract when treated with an equal part of a saturated nickel acetate solution, shows only the green color of the nickel salt; while the extracts of the other drugs all show decided color changes. On adding KOH solution this stays green, differentiating it still further from the others.

2. The residues from benzene solutions, originally orange yellow tint one, (senna is yellow and aloes orange yellow shade 2, while the others are red orange) when treated first with 1 cc. nitric and  $1/2$  cc sulfuric acid, then with an amount of  $\text{Na}_2\text{CO}_3$  not quite sufficient for neutralization, and reduction with stannous chloride, give a light red; while aloes, on similar



treatment is yellow orange, shade 2, and senna yellow, tint 1.

3. Rumex is to be distinguished in any series of reactions by the fact that its residues are lighter in color, and do not give as deep colors with the ordinary alkalies as the other drugs containing anthraquinones.

#### V. Rhubarb.

1. The benzene solution, when shaken with concentrated ammonia gives a precipitate, which on settling forms in a red violet layer between the benzene and the ammonia. The solution of the other drugs are clear, and, like rhubarb, a more or less deep red color.

2. The ether solution, plus an equal part of NiAc solution; when made alkaline with KOH gives a dark red violet precipitate which is like that from frangula, but the ether layer of the rhubarb solution becomes an intense red, while that from frangula retains its original color.

3. The resin from precipitation with an excess of water; when treated with sodium peroxide and alcohol, becomes red immediately, while the solutions of the other drugs develop little or no red color until water is added.

#### VI. Frangula.

Can be distinguished by the fact that it gives, in ether solution when treated with nickel acetate and KOH, a dark red-violet precipitate, in the water solution, leaving the ether layer uncolored. The precipitate from cascara treated in a similar way is dark orange red, and the layer above the precipitate in a rhubarb solution is deep red.

2. Amyl alcohol solutions of the fluid extracts of cascara



and frangula are red when treated with nickel acetate and KOH while the solutions of senna and rhubarb are orange, and those of rumex and aloes are yellow orange. Cascara may be distinguished from frangula by the fluorescence test with ammonia.

3. The stannous chloride reduction products, after evaporating ether and benzene solutions of frangula with nitric acid, are a much brighter violet-red than those from solutions of cascara and rhubarb treated in the same way, as well as much darker than the residue from rumex. The residues from senna and aloes show no red color.

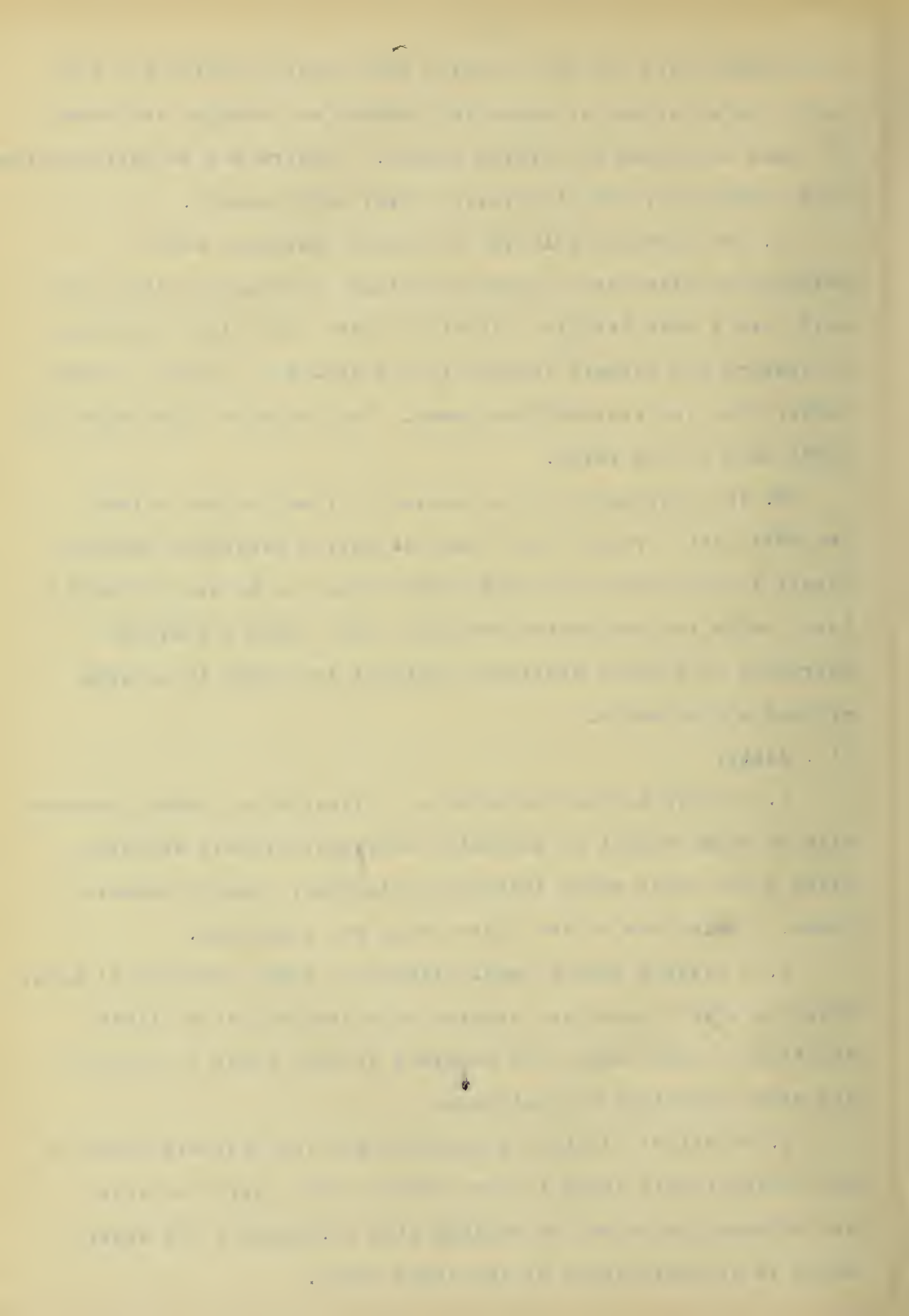
4. The sublimate from a residue of frangula has a very characteristic crystalline form; the entire sublimate forming itself in clusters of columns large enough to be seen without a lens, while the sublimates from the other drugs are either amorphous or contain scattered crystals too small to be seen without a microscope.

## VII. Aloes.

1. An amyl alcohol solution of a tincture of aloes, treated with an equal amount of saturated mercurous nitrate solution, gives a red color which deepens on standing, finally becoming brown. Solutions of the other drugs are colorless.

2. A residue from an amyl alcohol or ether solution of aloes; taken up with alcohol and treated with one drop of a dilute solution of  $\text{CuSO}_4$  and a few crystals of  $\text{NaCl}$  gives a red color. The other solutions are colorless.

3. Solutions of aloes evaporated and the residues taken up with alcohol this being in turn treated with cupric sulfate and hydrogen peroxide, on boiling give a raspberry red color, which is characteristic of the aloes alone.



## II. Outline of Procedure for Analysis:

1. Divide the Fluid extract to be examined into three parts.

(a) Shake out one portion with four times its volume of benzene, decant, and again shake out the lower layer with the same amount of amyl alcohol.

(b) Make a similar extract with the second portion of fluid extract, using ether as the solvent.

II. To the benzene solution apply the ammonia test for rhubarb.

III. To the amyl alcohol solution apply the ammonia test for cascara and aloes and the mercurous nitrate test for aloes. If this test gives positive results, confirm or deny the presence of cascara by the stannous chloride reduction of the benzene solution.

IV. To the ether solution apply the nickel acetate test, which will show the presence of senna, or of rumex, if the color of some other drug is not too dark to mask the colors.

V. If these tests have not served to show what the constituents of the solutions are, evaporate a portion of each solution, treat with nitric acid, stannous chloride, etc. checking the colors carefully with those shown in the charts for the pure fluid extracts, try the cupric sulfate test for aloes, and any other confirmatory tests that may seem necessary.



### III. Summary of Results

We have been able to find color reactions which will serve to detect the presence of rhubarb and cascara in almost any proportions in which they would be likely to be found in commercial fluid extracts. There were already several good tests for aloes, and we have been able to develop one other, - i.e., the mercurous nitrate test. On the other hand, while we have been able to find reactions which will serve to identify any one of the fluid extracts when it is pure, and we have found a very good test for senna in most mixtures; and several reactions which would show the presence of frangula if cascara or rhubarb were absent; we have not been able to find absolutely satisfactory tests for frangula and rumex; and our method for senna in the presence of some of the other drugs, especially rumex and frangula, involves the comparison of results from a series of tests in different solutions.

It is doubtful whether or not the sublimation tests will serve to detect any of these drugs in mixtures, since the other drugs present produce resins which would probably mask any characteristic form of a particular resin.



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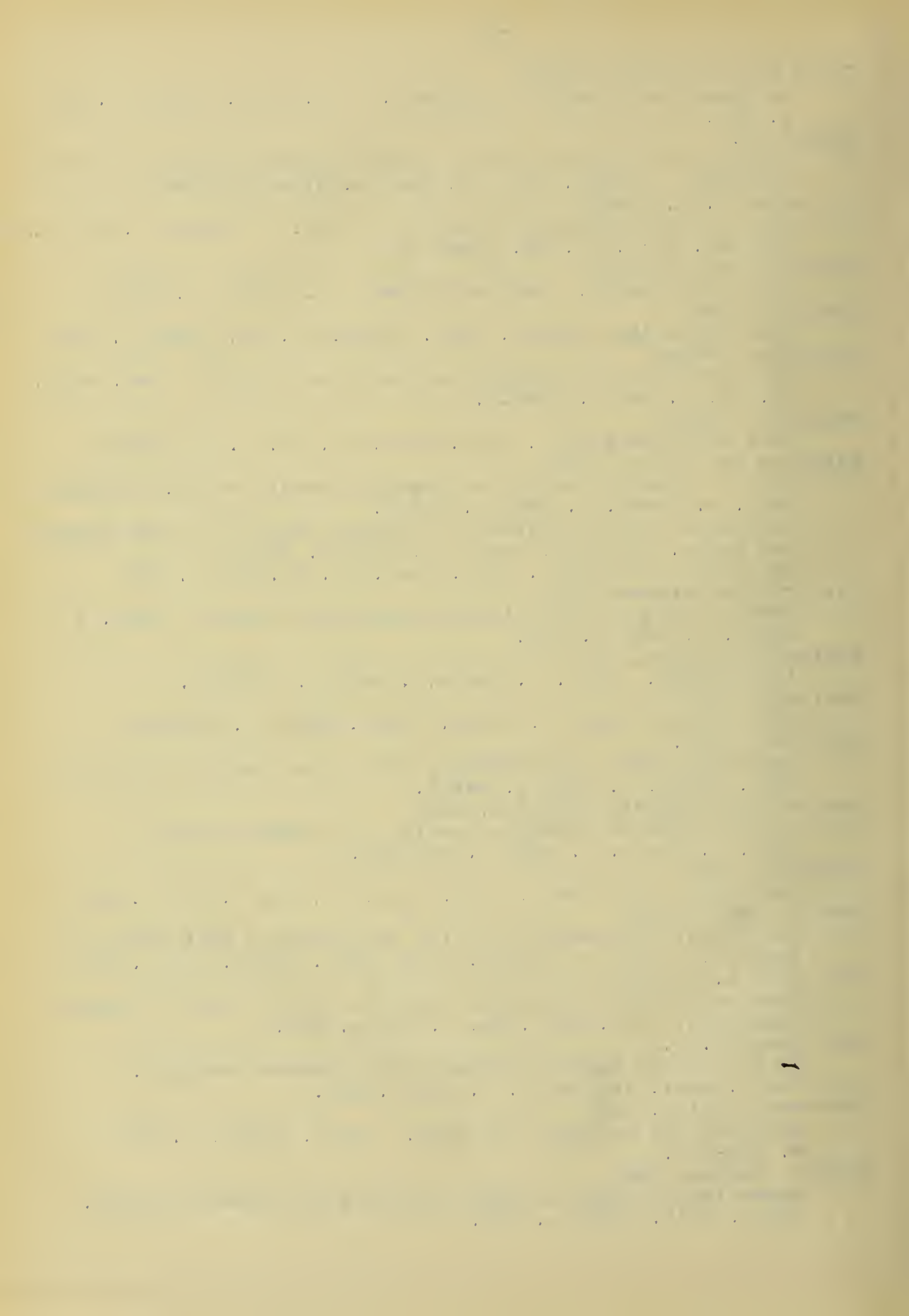
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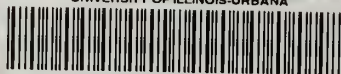
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